Cukurova Medical Journal
ÇUKUROVA ÜNİVERSİTESİ TIP FAKÜLTESİ

Cukurova Med J 2023;48(4):1293-1298
DOI: 10.17826/cumj.1354195

RESEARCH

Is insulin resistance a new comorbidity in seborrheic dermatitis: a case control study

İnsülin direnci seboreik dermatitte yeni bir komorbidite mi: bir vaka kontrol çalışması

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Abstract

Purpose: Seborrheic dermatitis (SD) is a chronic inflammatory skin disorder with an unknown etiology. Data from studies show that the prevalence of SD is higher in individuals with obesity. Insulin resistance (IR) is a metabolic condition characterized by high levels of insulin required to balance blood glycemia, and obesity is one of its clinical manifestations. This study presents one of the first prospective studies revealing the relationship between IR and SD in the literature.

Materials and Methods: In this case-control study, a total of 71 participants were included: 35 SD patients (15 males/20 females) and 36 controls (15 males/21 females). All participants were clinically evaluated for the presence or absence of seborrheic dermatitis by the same dermatologist. Parameters including HOMA-IR, insulin levels, serum lipid levels, waist circumference, and BMI were measured in both groups.

Results: HOMA-IR, insulin, total cholesterol, LDL cholesterol, waist circumference and BMI levels were higher in SD patients compared to the control group. Significant positive correlations were found between HOMA-IR and waist circumference, BMI, diastolic blood pressure, and triglyceride levels.

Conclusion: This study suggests that IR could be a new comorbid factor in seborrheic dermatitis. A substantial association was observed between SD and insulin resistance, possibly due to shared inflammatory pathogenesis. Consequently, individuals with SD should be monitored for insulin resistance-related conditions, emphasizing the importance of maintaining a healthy lifestyle.

Keywords: Seborrheic dermatitis, insulin resistance, comorbidity

Öz

Amaç: Seboreik dermatit (SD), etiyolojisi bilinmeyen kronik inflamatuar bir deri hastalığıdır. Mevcut çalışmalardan elde edilen veriler obezitesi olan bireylerde SD prevalansının daha yüksek olduğunu göstermektedir. İnsülin direnci (IR), kandaki glisemiyi dengelemek için gereken yüksek insülin seviyeleri ile karakterize edilen metabolik bir durumdur ve obezite bunun klinik belirtilerinden biridir. Bu çalışma literatürde insülin direnci IR ile SD arasındaki ilişkiyi ortaya koyan ilk prospektif araştırmalardan birini sunmaktadır.

Gereç ve Yöntem: Bu vaka-kontrol çalışmasına toplam 71 katılımcı dahil edildi: 35 SD hastası (15 erkek/20 kadın) ve 36 kontrol (15 erkek/21 kadın). Tüm katılımcılar aynı dermatoloji uzmanı tarafından seboreik dermatit varlığı veya yokluğu açısından klinik olarak değerlendirildi. Her iki grupta da HOMA-IR, insülin seviyeleri, serum lipit seviyeleri, bel çevresi ve vücut kitle indeksi (BMI) gibi parametreler ölçüldü.

Bulgular: SD'li hastalarda HOMA-IR, insülin, toplam kolesterol, LDL kolesterol, bel çevresi ve BMI düzeyleri kontrol grubuyla karşılaştırıldığında daha yüksekti. HOMA-IR ile bel çevresi, BMI, diyastolik kan basıncı ve trigliserit düzeyleri arasında anlamlı pozitif korelasyonlar bulundu.

Sonuç: Bu çalışma insülin direncinin IR'nin seboreik dermatitte yeni bir komorbid faktör olabileceğini düşündürmektedir. SD ile insülin direnci arasında muhtemelen ortak inflamatuar patogenezden dolayı önemli bir ilişki gözlendi. Sonuç olarak, sağlıklı bir yaşam tarzı sürdürmenin önemi vurgulanarak SD'li bireyler insülin direnciyle ilişkili durumlar açısından izlenmelidir.

Anahtar kelimeler: **S**eboreik dermatit, insülin direnci, komorbidite

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Received: 02.09.2023 Accepted: 03.12.2023

INTRODUCTION

While many infectious diseases in the world have been successfully treated with the use of antibiotics, many non-contagious diseases, the cause of which is often not fully identified, have become the main cause of illness and death for the entire world population[1]. Seborrheic dermatitis (SD) is a skin disease that involves chronic inflammation in its etiology, although its cause is still unknown today. There is no specific treatment for SD, although some data suggest that SD is more commonly seen in individuals with obesity[2]. Cutaneous lesions of SD are more frequently observed in areas where sebaceous glands are densely packed[3]. SD is seen in both infancy and adult age group[3].

Insulin resistance (IR) is a metabolic condition that requires a high insulin hormone level to counteract the glycemia of the blood. Clinical manifestations of IR include abdominal obesity, fatty liver, polycystic ovary syndrome, metabolic syndrome (MS), and obstructive sleep apnea. Also MS known as "insulin resistance syndrome" or "syndrome X" is a cluster of conditions, including dyslipidemia, hypertension, abdominal obesity, and high blood glucose, that together raise the risk of several serious health problems such as cardiovascular diseases, type 2 diabetes, and even death[4]. IR has dermatological manifestations; one of these is a well-known condition called acanthosis nigricans[5]. Another dermatological pathology associated with IR is psoriasis, an inflammatory condition similar to SD[6].

Some studies in the literature have revealed a relationship between MS and SD[7]. However, data related to IR is missing. This study is one of the first prospective investigations demonstrating the relationship between IR and SD in the literature. With this study, we investigated the relationship between IR, which is an important cause of morbidity today, and an inflammatory disease such as SD, which we frequently encounter in our daily dermatology practice. Our aim is to predict significant morbidity and take steps to prevent it.

MATERIALS AND METHODS

Sample

This case prospective-control study was conducted in the Giresun University Departments of Endocrinology and Metabolism and Dermatology. A population of 56 patients, who applied to Giresun University Training and Research Hospital in 2022, diagnosed clinically with SD wasincluded in our study group. Based on the article, it is necessary to conduct research on 14 cases according to the results of chi-square test power analysis with 95% confidence (1-α), 95% test power (1-β), w = 0.320 effect size. 4 groups were determined with 14 patients in each group with the power analysis performed before the study. Patients in both groups were evaluated by the same specialists in daily practice of Giresun University Training and Research Hospital Departments of Dermatology and Endocrinology and Metabolism; those with and without (control group) seborrheic dermatitis. The diagnosis of seborrheic dermatitis was established after a comprehensive clinical evaluation of the entire body based on its clinical features. The control group consisted of healthy volunteers matched for age and sex, who were accepted for nevus screening. Informed consent was obtained from all participants included in our study.

Exclusion criteria included the presence of diabetes mellitus (antidiabetic medicine usage and/or biochemical diagnosis of DM on hospital records), cardiac failure, hepatic failure, renal failure, malignancy, rheumatic disorder and usage of any drug effecting insulin resistance, and presence of pregnancy. Fasting glucose lower than 126 mg/dl (according to American Diabetes Association) were accepted as non-diabetic and age between 18-90 years old were included into the study. Individuals in the control group had no history of medication, nutritional supplement use or diabetes. This study commenced after receiving approval from the Ethics Committee (Ethics Committee No: KAEK-59) of the Clinical Research Ethics Committee at Giresun University Faculty of Medicine. Additionally, written informed consent was obtained from all participants. All procedures in this study were conducted in accordance with the ethical standards of the institutional and/or national research committee and followed the Declaration of Helsinki[8].

Measurements

The subjects' weight, height, systolic blood pressure (SBP), and diastolic blood pressure (DBP) values were measured by same endocrinologist. BMI was calculated as weight in kilograms divided by height squared in meters (kg/m^2). After a 12-hour fasting period, 5 ml of blood was drawn into vacuum plain

tubes. Then blood tubes were centrifuged at 1500 g for 10 minutes. Serum were stored at -80 Celsius refrigerator. Serum triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and fasting plasma glucose (FPG) levels were measured using the photometric method in a chemistry autoanalyzer (Roche Cobas C 311, Roche Diagnostics Ltd. CH-6343 Rotkreuz, Switzerland). Serum insulin levels were determined using the electrochemiluminescence method (Roche Cobas e 411 immuno analyzer, Roche Diagnostics Ltd. CH-6343 Rotkreuz, Switzerland). All test were performed in biochemistry laboratory.

Homeostasis model assessment of IR (HOMA-IR) was calculated by multiplying the fasting insulin value (μIU/mL) by the plasma glucose concentration value (mg/dL) and then divided by 405. An HOMA-IR value greater than 2 was considered indicative of insulin resistance[9].

Statistical analysis

The data used in our study were shown as the median value (interquartile range). Anomaly in the data was analyzed using Sapiro wilk and Kolmogorov-Smirnov tests. Also; Kurtosis and skewness tests were performed for determining normality of variables. The Nonparametric Mann-Whitney U test was used between SD and control. Median and 25-75 SD percentiles were presented. The relationship between clinical and laboratory variables was analyzed using non-parametric methods (Two tailed Spearman correlation test). $P < 0.05$ was defined as threshold value. All statistical analyzes were performed with the aid of SPSS 21.0 for Windows (SPSS, Inc, Chicago, Illinois, USA).

RESULTS

35 SD and 36 control were included in the study. There was no statistical difference between groups in terms of age and gender (Table-1). HOMA-IR, insulin, total cholesterol, LDL cholesterol, waist circumference and BMI were higher in patients with SD compared to control group (Table 2). Systolic blood pressure and diastolic blood pressure were same between groups (Table 2). Spearman's correlation analysis were performed for evaluating clinical and laboratory parameters. There were significant positive correlation between HOMA-IR and waist circumference, BMI, diastolic blood pressure, triglyceride (Table 3). There were negative correlation between waist circumference and HDL cholesterol (Table 3). Also positive correlation were detected between waist circumference and total cholesterol LDL cholesterol, HDL cholesterol, triglyceride, Also systolic and diastolic blood pressure were positively correlated with waist circumference, total cholesterol, triglyceride, LDL cholesterol and serum glucose level (Table 3). Insulin resistant cases were more commonly observed between SD groups (Table 4).

Table 1. Demographic parameters of the cases

	Seborreic dermatic	Control	P value
Age (% Persentil 25-75)	35 (25.75-45.75)	36 (27-42)	P=0.88
Gender (M/F) (percent)	15/20 (42.9/57.1)	15/21 (41.7/58.3)	p=0.55

*Data were evaluated with Chi-square test. M=male, F=Female

Table 2. Clinical and biochemical parameters of the cases.

	Seborheic dermatit	Control	P value
HOMA-IR*	2.77 (2.15-4.11)	2.32 (1.42-2.93)	0.016
Insulin	12.74 (9.55-16.04)	10.26 (6.23-12.71)	0.010
Glucose	94 (89,5-100)	92 (89-96)	0.400
Total cholesterol	194.5 (170,5-219,25)	179 (158-191)	0.034
Triglyceride	119.5 (84-161.25)	90 (66-155)	0.083
LDL cholesterol	122.5 (93-143.25)	104 (87-117)	0.042
HDL cholesterol	48.50 (41-56,5)	51 (44-66)	0.223
BMI	26.22 (24.3-31.25)	25.66 (22.77-28.91)	0.151
Waist circumference	100.5 (88-106.25)	90 (78-98)	0.034
SBP**	120 (110-140)	120 (110-125)	0.108
DBP***	80 (77.5-90)	80 (70-80)	0.008

Data were evaluated with nonparametric Mann Whitney U test. Median values with % 25-75 percentiles were presented.
*HOMA-IR=Homeostatic assessment of insulin resistance, **SH=Systolic blood pressure, ***DBP=Diastolic blood pressure

Table 3. Correlation analysis between HOMA-IR and various parameters.

Parameters		HOMA-IR	Waist Circumference	Systolic blood pressure	Diastolic blood pressure
Waist(cm)	r	0.381	-	-	-
	p	0.001	-	-	-
BMI	r	0.368	-	-	-
	p	0.002	-	-	-
Systolic blood pressure	r	-	0.375	-	-
	p	-	0.001	-	-
Diastolic blood pressure	r	0.265	0.526	-	-
	p	0.026	0.001		-
Glucose (mg/dl)	r	-	-	0.479	0.455
	p	-	-	0.001	0.001
TC (mg/dL)	r	-	0.446	0.428	0.478
	p	-	0.001	0.001	0.001
TG (mg/dL)	r	0.435	0.432	0.337	0.337
	p	0.001	0.001	0.005	0.005
LDL-C (mg/dL)	r	-	0.459	0.440	0.456
	p	-	0.001	0.001	0.001
HDL-C (mg/dL)	r	-0.356	-0.368	-	-
	p	0.003	0.002	-	-

Table 4. Frequency of insulin resistance between groups

	Seborreic dermatic	Control	P value
High HOMA-IR index	28	19	P=0.015
Normal HOMA-IR index	7	17	

HOMA-IR: The homeostasis model assessment of insulin resistance

DISCUSSION

The main finding of our study is a higher frequency of insulin resistance in the SD group. Another result of this study is that increasing in waist circumference and diastolic blood pressure in SD patient. As we know SD is a chronic inflammatory dermatological disorder with an unknown etiology. Despite numerous theories proposed regarding its cause, definitive results have not been obtained to date. The possible etiologies include seborrhea and Malassezia. SD primarily affects the scalp, eyebrows, and nasolabial folds and has been identified as a predictive factor for the development of metabolic syndrome[7]. Although it is well known that skin diseases involving chronic inflammation in their etiology are closely related to comorbidities such as metabolic syndrome, obesity, cardiovascular diseases (CVD) and diabetes, it has also been demonstrated by an increasing number of studies. Nowadays, a limited number of authors have started to investigate the relationship between SD and metabolic syndrome, hypertension, obesity, and various nutritional factors[10].

But there are only a few studies that have investigated glucose and insulin levels in SD patients[11]. In one of these studies, Erdoğan et al. showed significantly higher fasting plasma insulin levels, HOMA-IR and OGTT 2-h PG in the SD group compared with the control group. Additionally, the number of individuals with IR was significantly higher in the SD group compared to the control group[12]. Similarly our study also showed that increased IR levels in patients with SD.

Two other studies from Türkiye investigated a relationship between metabolic syndrome (MS) and SD. One of them, studied by Imamoglu et al.,

revealed a significant correlation between disease severity and plasma HDL levels. They also found a relationship between first-degree relatives in both SD and control groups with a history of metabolic disease or any syndrome in their families[7]. Another study from the same country by Akbaş et al. demonstrated that the presence of MS and high systolic and diastolic blood pressure were observed more frequently in SD patients than in the control group[13]. In the present study, we found only higher total cholesterol and LDL cholesterol levels in SD patients. Also a relationship was found between SD and diastolic blood pressure levels of control group in our study. Similarly a study which was studied in Iran, found that systolic and diastolic blood pressure and waist circumference in case group were more than in control group but just systolic blood pressure and waist circumference were statistically significant. They also found HDL levels in the patient group were statistically significantly lower than in the controls and mean of triglyceride, cholesterol, LDL, fasting blood glucose (FBS), in case group were more than in control group but not statistically significant. Additionally in case group 20.5% and in control group 7.7% were afflicted metabolic syndrome which was not statistically significant[14]. Similar results to our study reveal the importance of the need for further studies, especially in terms of the relationship between arterial blood pressure and waist circumference and SD.

Inflammatory markers have been shown to be increased in dermal biopsy material from SD patients, including interleukins, interferon gamma, and tumor necrosis factor alpha (interleukin-1 [IL-1], IL-1β, IL-2, IL-4, IL-6, IL-10, IL-12, gamma interferon [IFN-γ], and tumor necrosis factor alpha [TNF-α]). Skin biopsies of SD patients revealed elevated inflammatory markers through immunohistochemistry in the epidermis surrounding diseased follicles[15]. These markers are similar to those produced by Malassezia yeasts in experimental models. Malassezia restricta is a commonly isolated yeast from human skin, shown to increase inflammatory markers such as interleukins, interferons, and tumor necrosis factor alpha in patients' skin specimens. However, the net effect of this cytokine synthesis could not be determined from human data in the literature[16].

These inflammatory mediators play a significant role in the development of insulin resistance. In insulin-resistant individuals, IL-10 serum levels were found to be increased compared to healthy individuals. Inflammatory markers like TNF-alpha and IL-1 may be related to chronic low-grade inflammation[17]. Chronic inflammation is a main component of IR and visceral adiposity[18]. In a study conducted in our country, while investigating the relationship between inflammatory blood parameters and seborrheic dermatitis, the Seborrheic Dermatitis Area Severity Index (SDASI) score was calculated in every SD patients. The findings revealed that there was a significant correlation between CRP and red cell distribution width (RDW) as well as age with SDASI score[19]. One of the limitations of our study could be the omission of calculating the severity score in patients with seborrheic dermatitis.

Additionally, apart from associated comorbid conditions, evaluating body composition parameters such as height, weight, BMI, fat mass, metabolic age, body density, visceral adiposity, mineral, and protein levels can be crucial in inflammatory diseases. A study investigating body composition parameters and SD showed no significant difference between the two groups[8]. The other limitation is more meaningful results could have been achieved by evaluating the metabolic parameters in our study with the body composition parameters of the patients.

Limitations: Severity score of SD is the limitations of the study. The other limitation is the absence of comparison of IR in SD and control groups with similar BMI and waist circumference. This is because of limited number of study population.

IR appears to be a novel candidate component of SD. Our study reveals a robust association between SD and insulin resistance, potentially stemming from similar inflammatory pathogenesis. As a result, patients with SD should be monitored for conditions related to IR and encouraged to maintain a healthy lifestyle. Additionally more new studies with larger sample sizes for patients are needed to explain the relationship between this parameters. Further research with a larger sample size and evaluating inflammatory markers related with SD will add to clarify is necessary to substantiate this hypothesis.

Author Contributions: Concept/Design : BA, OD; Data acquisition: BA, OD; Data analysis and interpretation: BA, OD; Drafting manuscript: BA, OD; Critical revision of manuscript: BA, OD; Final approval and accountability: BA, OD; Technical or material support: BA, OD; Supervision: BA, OD; Securing funding (if available): n/a.
Ethical Approval: Ethical approval was obtained from the Giresun University Clinical Research Ethics Committee with the decision dated 15.11.2017 and numbered 08/4.
Peer-review: Externally peer-reviewed.
Conflict of Interest: Authors declared no conflict of interest.
Financial Disclosure: Authors declared no financial support

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